Author's response to reviews

Title: Treatment of locally advanced carcinomas of head and neck with intensity-modulated radiation therapy (IMRT) in combination with cetuximab and chemotherapy: the REACH protocol

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Dear Editor,

enclosed, please find the revised version of the above listed manuscript suggested for publication in BMC Cancer. The manuscript has undergone thorough revision according to the valuable suggestions made by the reviewers and we believe that this has considerably improved the quality and merit of our manuscript.

In the following I would like to address and respond to each point made by the reviewers.

Reviewers' comment:
However, in the version provided for review, several sections outlined in the instructions for authors for a study protocol submission are missing, in particular a title page and an abstract (including the trial registration number). These should be added in a revised version of the manuscript.

Answer:
We added the already existed title page and the abstract within the trial registration number.

Editor's comment:
Please provide a Title Page within your manuscript file. This should list: the title of the article, which should include an accurate, clear and concise description of the reported work, avoiding abbreviations; and the full names, institutional addresses, and e-mail addresses for all authors. The corresponding author should also be indicated.
Answer:
The mentioned title page is added. See comment above.

Reviewer's comment:
Please provide your Abstract within your manuscript

Answer:
The abstract is added to the manuscript.

Reviewer's comment:
Please include a 'Competing interests' section between the Conclusions and Authors' contributions. If there are none to declare, please write 'The authors declare that they have no competing interests'.
The questions that are asked of authors are:
Financial competing interests
* In the past five years have you received reimbursements, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future? Is such an organization financing this manuscript (including the article-processing charge)? If so, please specify.
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* Do you hold or are you currently applying for any patents relating to the content of the manuscript? Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript? If so, please specify.
* Do you have any other financial competing interests? If so, please specify.
Non-financial competing interests
* Are there any non-financial competing interests (political, personal, religious, academic, ideological, intellectual, commercial or any other) to declare in relation to this manuscript? If so, please specify.

Answer:
We included the sentence (page 11)
“Competing interests
The authors declare that they have no financial or non-financial competing interests.”

In particular, we declare that we have none of the above mentioned competing interests.

Reviewer's comment:
Please provide a power calculation within the Methods section.

Answer:
We added the sample size calculation and the statistical methods to page 9.

„Sample Size Calculation
The choice of number of patients is based on pragmatic reasons. Therefore, the sample size analysis is replaced by a power analysis giving the expected accuracy of the results.
It is estimated that the two-year Local Regional Control rate will be 75 per cent. Given a constant hazard rate over time (leading to an exponential distribution), and assuming a two-year accrual time and a three-year follow-up time (leading to a median observation time of less than four years), with 60 patients treated the three-year LRC rate can be estimated with a 95%-confidence interval of approximate width of 18 per cent, i.e. if the LRC estimate is 65 per cent, the limits can be expected to be at 53 and 81 per cent.

**Statistical Methods**

The time to event for local regional control, disease-free survival, progression-free survival, overall survival will be calculated using a Kaplan-Meier estimate, along with a 95 per cent confidence interval.

Acute and late radiation effects as well as adverse events will be tabulated and listed by seriousness, severity, System Organ Class and relatedness.

Biometric analysis will be specified in more detail in the statistical analysis plan which has to be authorized before opening the database for analysis by the biometrician, the sponsor, and the LKP.”